

<b>Policy Name:</b>	<b>Expanded Carrier Testing for Genetic Diseases in Adults</b>
<b>Effective Date:</b>	<b>1/18/2021</b>

## Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica plans. Please refer to the member's plan document for specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare and Minnesota Health Care Programs, this policy will apply unless those programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

## Coverage Policy

Carrier testing using a limited genetic panel for individuals of Ashkenazi Jewish ancestry is **COVERED** when all the following are met:

1. Screening is done for the disorders as recommended by the American College of Medical Genetics (ACMG) and the American College of Obstetricians and Gynecologists (ACOG). The following conditions reflect the emerging clinical and scientific evidence for carrier testing in this population as of guideline publications dates, and include:
  - a. Tay Sachs disease
  - b. Canavan disease
  - c. Cystic fibrosis
  - d. Familial dysautonomia
  - e. Bloom syndrome
  - f. Familial hyperinsulinism
  - g. Fanconi anemia group C
  - h. Gaucher disease
  - i. Glycogen storage disease type I
  - j. Joubert syndrome
  - k. Maple syrup urine disease
  - l. Mucopolysaccharidosis IV
  - m. Niemann-Pick disease
  - n. Usher syndrome.
2. Medical records document confirmation of Ashkenazi Jewish ancestry and genetic counseling by a medical geneticist, a certified and licensed (where required) genetic counselor not associated with the laboratory performing the testing, or a sub-specialist in maternal-fetal medicine.
3. The individual is currently pregnant or contemplating pregnancy.
4. The test will affect reproductive choices.

Expanded carrier testing for genetic diseases is investigative and therefore **NOT COVERED**. Tests include, but are not limited to:

1. Carrier Status DNA insight
2. CarrierMap
3. Counsyl Foresight Carrier Screen
4. GeneAware Panels
5. GoodStart™ Inherigen™, InherigenPlus™, InherigenTx
6. Inheritest™
7. Invitae Carrier Screens (e.g., Broad and Comprehensive)
8. Natera Horizon™ Multi-Disease Carrier Screening
9. NxGen MDx Carrier Panels
10. Otagenetics Gene Tests
11. Pathway Carrier Status DNA Insight™
12. Progenity™ Pan-Ethnic Carrier Screening
13. QHerit
14. 23andMe.

There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the safety and efficacy or effects on health care outcomes.

Note: See also related Medica coverage policy, *Genetic and Pharmacogenetic Testing*.

## **Description - What is it and how is it used?**

Traditional carrier testing is done with targeted single gene screening associated with one disease (e.g., the cystic fibrosis transmembrane conductance regulator [CFTR] gene for cystic fibrosis). However, new methodologies have allowed for expanded carrier testing panels intended to identify genes representing multiple and generally unrelated disorders/conditions. This expanded testing is considered a non-targeted approach to carrier testing. Testing is done using buccal swabs, saliva, or blood specimens. These expanded carrier screening tests vary in their size, scope, and technologies used. The Counsyl Foresight Carrier Screen website has limited information on the specific testing methodologies used and lists full exon sequencing, targeted sequencing, custom assays, and panel-wide deletions as the methodologies utilized. Often, these methods employ next generation sequencing (aka massively parallel or high-throughput sequencing) or microarray analysis.

Certain identified autosomal recessive diseases/conditions are more prevalent in individuals of Ashkenazi Jewish ancestry. Both the American College of Medical Genetics (ACMG) and American College of Obstetricians and Gynecologists (ACOG) recommend that carrier testing in this population be done for Tay-Sachs disease, Canavan Disease, and familial dysautonomia. In addition, ACOG recommends testing for cystic fibrosis. Also, both ACMG and ACOG recommend that individuals inquire about and be offered testing for other conditions directly linked to Ashkenazi Jewish ancestry, including Franconi anemia group C, Niemann-Pick disease type A, mucopolipidosis IV, Bloom syndrome, and Gaucher disease. The basis for these recommendations is the high detection rates which currently available tests offer, resulting in a carrier detection rate of greater than or equal to 95% for the majority of these disorders. As a result, the expected mutation-specific carrier frequencies are relatively high even for those identified disorders that are less common.

Currently, there is no standardization between similar expanded carrier genetic panels, with tests performed by different laboratories for the same conditions/diseases often testing different sets and combinations of genes. In addition to testing for standard conditions, expanded carrier testing includes many conditions that: (1) are not routinely evaluated, (2) are not addressed in professionally recognized guidelines, (3) have a low prevalence in the general population (i.e., the individual is at very low risk of being a carrier), or (4) have no known treatment. A description of a selection of available extended carrier testing panels follows:

1. **Counsyl Foresight Carrier Screen:** Counsyl website states the Family Prep Screen tests for carrier status of 107 disorders using a proprietary multiple molecular inversion probe assay. The diseases tested are purported to lead to shortened life spans, have limited treatment options, or can lead to intellectual disability.
2. **GeneVu Carrier Screening:** Invitae/GoodStart Genetics customizes a testing panel for each individual based on ethnicity, family history, and provider testing preferences. The test panels are comprised of carrier testing for selected pan-ethnic conditions (e.g., cystic fibrosis, spinal muscular atrophy, fragile X syndrome), hemoglobinopathies (e.g., alpha-thalassemia, beta-thalassemia, and sickle cell disease), and up to 19 Ashkenazi Jewish disorders.
3. **Inherigen:** The comprehensive panel tests for over 180 pan-ethnic inherited diseases (720 mutations) that are typified by childhood onset accompanied by severe symptoms (e.g., immunodeficiencies) and many metabolic diseases (e.g., fatty acid oxygenation, glycogen storage diseases, Tay Sachs disease). The Inherigen Plus tests for all diseases described above with the addition of cystic fibrosis, spinal muscular atrophy, and Fragile X syndrome. InheriGenTx is a comprehensive multi-gene panel designed to screen for mutations that could result in 75 hereditary diseases that can be life-altering, but for which effective treatment/management options are available. The Ashkenzi Jewish carrier screening panel test for more than 45 disorders.
4. **Inheritest:** The comprehensive panel tests for over 110 pan-ethnic autosomal recessive conditions/diseases. The Inheritest Select Carrier Screen tests for 18 diseases associated with individuals of Ashkenazi Jewish ethnicity.
5. **Natera Horizon™ Multi-Disease Carrier Screening:** This expanded carrier testing panel tests for up to 274 autosomal-recessive and X-linked genetic conditions.
6. **23andMe:** This panel was previously marketed as a saliva-based direct-to-consumer (DTC) personal genome test. In 2013 the FDA required 23andMe to discontinue marketing its personal genome service based on failure to obtain legally required regulatory approval. The FDA stated concerns about the potential consequences of individuals receiving inaccurate health results. In the United States, 23andMe continues to markets a personal genome test, but does not report health-related results. 23andMe markets both ancestry and health-related tests in Canada and in the United Kingdom.

## Background:

Each of the twenty-three human chromosomes is composed of two DNA strands, with genes interspersed along each chromosome. An allele is an alternative form of a gene found at the same place on both strands of the chromosome, one allele arising from the father and one from the mother. When a mutation occurs within one of these alleles, disease may result. The affected allele may show dominant, recessive, or X-linked inheritance patterns. Normally, a dominant allele produces a disorder/disease in an individual who has inherited only one copy of the allele from one parent. For a recessive allele to produce the disorder/disease, the individual must inherit two copies of the abnormal allele, one from each parent.

A carrier of an allele associated with recessive inheritance carries one abnormal genetic allele for the disorder/disease but does not display symptoms for the defined condition. Carrier testing is usually performed on couples to determine the possible risk of passing a recessive inheritance pattern disorder/disease on to their offspring. Carrier testing may be performed for conditions that are found in the general population (i.e., pan-ethnic conditions), for diseases that are more commonly associated with a particular population (i.e., ethnicity-related conditions), or when a family history might suggest the presence of a disease associated with genetic inheritance. When both parents carry an autosomal (i.e. non-X or non-Y chromosome) recessive allele or one parent carries an X-linked allele, there is a 25% chance that an offspring will inherit the disorder/disease.

## **FDA Approval**

Laboratory tests are regulated under the Clinical Laboratory Improvement Amendments (CLIA) Act of 1988. Premarket approval from the FDA is not required as long as the assay is performed in a laboratory facility that observes CLIA regulations and the assay is not marketed for general use. Currently, no expanded carrier tests in adults have received FDA approval. Examples of available proprietary tests include, but are not limited to:

1. Counsyl Foresight Carrier Screen (Counsyl, Inc.)
2. GeneVu Carrier Screening (Invitae/GoodStart Genetics)
3. Inherigen™ (GenPath)

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4. Inheritest™ (Integrated Genetics/LabCorp Specialty Testing Group)
5. Natera Horizon™ Multi-Disease Carrier Screening (Natera)
6. 23andMe (23andMe)

### Prior Authorization

Prior authorization is not applicable. Claims for this service are subject to retrospective review and denial of coverage, as investigative services are not eligible for reimbursement.

### Coding Considerations

Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

#### CPT Codes:

81412 - Ashkenazi Jewish associated disorders (eg, Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1

Original Effective Date: 5/1/2012

Re-Review Date(s): 3/18/2015  
1/4/2016 – administrative update; code added  
3/21/2018  
2/10/2020 – administrative update; format  
11/18/2020

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